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A rational approach for ω-transaminase-catalyzed process design: synthesis of p-Br-1-phenylethylamine

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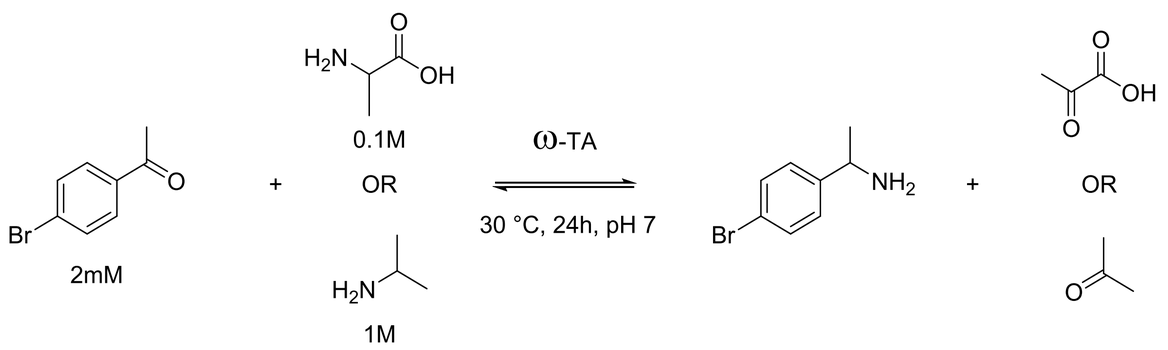
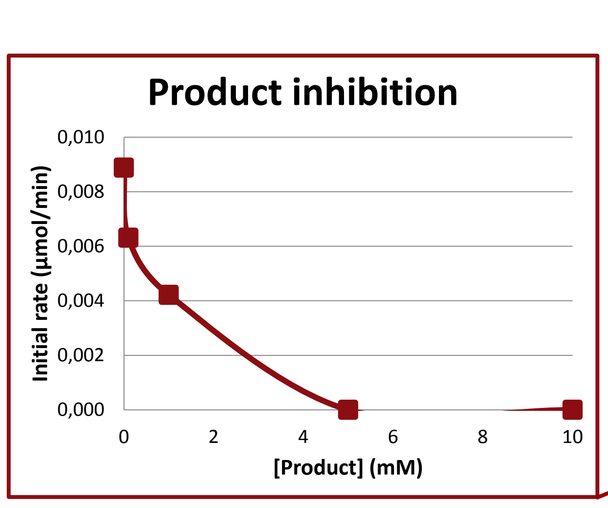
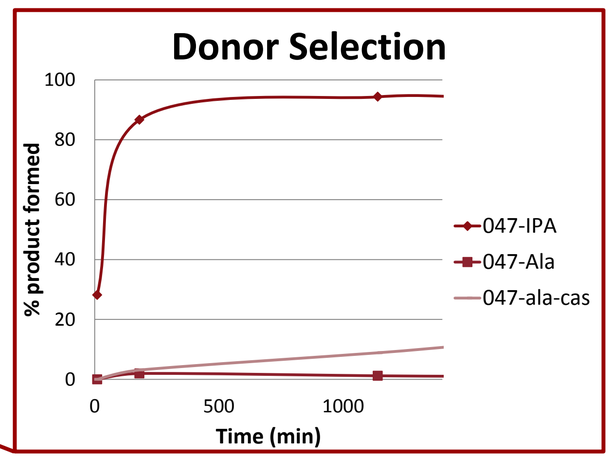
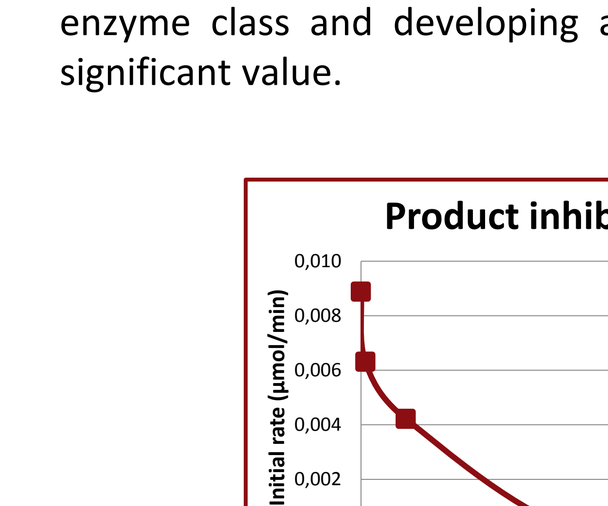
Introduction

Herein we describe a novel rational approach to the design of a ω-transaminase process such that it will fulfill criteria necessary for industrial use. By first determining the fundamental properties of the reaction system, it is possible to suggest appropriate process strategies that may be used to overcome any unfavorable parameters. The ω-transaminase is used as a model system because it is an important enzyme class and developing a systematic methodology would have significant value.









Kinetics

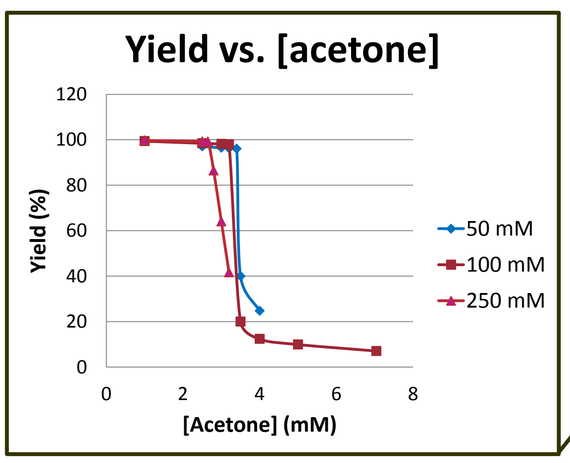
Biocatalyst

Assessment and Process design

Thermo-dynamics

$$K_{eq} = \frac{[product][co-product]}{[Acceptor][donor]} = \frac{[1,89][1,89]}{[0,11][998,11]} = 1/30$$

Parameter	Acceptor	Product
Water solubility	2mM	15mM
Boiling point	255 °C	?



- Co-product removal
  - Acetone stripping
  - Cascade reaction
- Product removal
  - Extraction
    - Resins
    - Organic solvents
  - Precipitation
    - pH change
    - Organic solvents

Product precipitation may be induced by a pH change or by using a polar solvent.

Discussion

It is clear that the reaction studied exhibits many of the challenges often found with the use of transaminases for the synthesis of pharmaceutical intermediates such as product inhibition, unfavorable thermodynamics and poor solubility. We here propose a number of process strategies which, if adopted additively, may make the process economically viable.

Acknowledgements

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